General

Guideline Title

PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation.

Bibliographic Source(s)

Seem DL, Lee I, Umscheid CA, Kuehnert MJ, United States Public Health Service. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep. 2013 Jul;128(4):247-343. PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rogers MF, Simonds RJ, Lawton KE, Moseley RR, Jones WK. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. MMWR Recomm Rep 1994;43(RR-8):1-17.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The categorization scheme applied to recommendations (categories IA, IB, IC, ID, IIA, and IIB) is provided at the end of the "Major Recommendations" field.

Risk Assessment (Screening) of Living and Deceased Donors

1. All living potential donors and individuals interviewed about deceased potential organ donors (e.g., next of kin, life partner, cohabitant, caretaker, friend, or primary treating physician) should be informed of the donor evaluation process, including the review of medical and behavioral history, physical examination, and laboratory tests to identify the presence of infectious agents or medical conditions that could be transmitted by organ transplantation. (Category ID)

2. To ascertain whether potential organ donors are at increased risk for human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) infection, living donors, or individuals contacted about deceased donors, should be interviewed in a confidential manner about behaviors that may have increased the potential donor's probability of having HIV, HBV, or HCV infection. (Category IB)

3. Living potential donors with behaviors associated with an increased risk of acquiring HIV, HBV, or HCV identified during evaluation should receive individualized counseling on specific strategies to prevent exposure to these viruses during the time period prior to surgery. (Category ID)

4. If a potential donor is ≤18 months of age or has been breastfed within the preceding 12 months, the birth mother, if available, should be

interviewed about behaviors that may have placed her at risk for HIV, HBV, or HCV infection. (Category IB)

5a. When a deceased potential organ donor's medical/behavioral history cannot be obtained or risk factors cannot be determined, the donor should be considered at increased risk for HIV, HBV, and HCV infection because the donor's risk for infection is unknown. (Category ID)

5b. When a deceased potential organ donor's blood specimen is hemodiluted, the donor should be considered at increased risk for HIV, HBV, and HCV infection because the donor's risk for infection is unknown. (Category IB)

Testing of Living and Deceased Donors

6. All living potential donors should be tested for HIV, HBV, and HCV as close as possible to the date of the organ recovery operation, but at least within the 28-day time period prior to surgery. (Category ID)

7. All potential organ donors (living or deceased) should be tested for antibodies to HIV (i.e., anti-HIV 1/2 or HIV antigen/antibody [Ag/Ab] combination assay). All potential organ donors identified as being at increased risk for HIV infection should also be tested for HIV ribonucleic acid (RNA) by nucleic acid test (NAT) or HIV antigen (e.g., HIV Ag/Ab combination assay). Donor blood specimens should be obtained before procurement. Ab or Ag/Ab test results should be made available before transplantation. (Category IB) (Note: Optimally, all NAT results for deceased donors should be available before the transplant occurs; however, if having NAT results before transplantation is not feasible, test results can be useful to guide recipient treatment.)

8. All potential organ donors (living or deceased) should be tested for both anti-HCV and for HCV RNA by NAT. Donor blood specimens should be obtained before procurement. Ab test results should be made available before transplantation. (Category IB) (Note: Optimally, all NAT results for deceased donors should be available before the transplant occurs; however, if having NAT results before transplantation is not feasible, test results can be useful to guide recipient treatment.)

9. All potential organ donors (living or deceased) should be tested for antibody to hepatitis B core antigen (anti-HBc) and for hepatitis B surface antigen (HBsAg). Donor blood specimens should be obtained before procurement. Ab/Ag test results should be made available before transplantation. (Category IB)

Refer to Figures 4 and 5 in the original guideline document for recommended donor tests for deceased and living donors, respectively.

Informed Consent Discussion with Transplant Candidates

10. An informed consent process discussion between the transplant candidate, or medical decision maker, and the listing clinician should start before the patient is placed on the transplant wait list. Patients should be counseled to consider potential risks of both accepting and rejecting organs from donors known to be infected with HBV or HCV, or donors at increased risk for HBV, HCV, or HIV infection. (Category IB)

11. The transplant candidate, or medical decision maker, should have opportunities to discuss with clinicians issues related to the associated risk of HIV, HBV, or HCV transmission with organ acceptance while the patient is on the transplant wait list. (Category IB)

12. At the time of the organ offer, if a donor is identified as being at increased risk for HIV, HBV, or HCV infection, the transplant center team primarily responsible for the patient's care should include this risk information in the informed consent discussion with the transplant candidate or medical decision maker. (Category IB)

13. If prior to transplantation or repair of a transplanted organ it is known or anticipated that stored blood vessel conduits (from a donor who is different from the donor of the primary organ being transplanted or repaired) may be used, and the donor is identified as being at increased risk for HIV, HBV, or HCV infection, then the transplant center team should include this risk information in the informed consent discussion. (Category IB)

14. When organs from HBV- or HCV-infected donors will be used, the transplant center team primarily responsible for the patient's care should have an informed consent discussion with the transplant candidate, or medical decision maker, prior to transplantation regarding the risks related to disease transmission. (Category IB)

15. Transplant candidates should be informed that although all donors are screened for HIV, HBV, and HCV, donor screening has limitations and no screening question or laboratory test can completely eliminate the risk for transmitting these infections (or any other infection). (Category IB)

Testing of Recipients Pre- and Posttransplant

16. Pre-transplant testing of transplant candidates for HIV, HBV, and HCV should be conducted when the donor (living or deceased) meets any of the following conditions: (1) identified as being at increased risk for HIV, HBV, and HCV infection (Note: If the donor is only identified as being at risk for HCV infection due to hemodialysis in the preceding 12 months, then testing for HCV only is recommended); (2) screening specimens

are hemodiluted; or (3) the medical/behavioral history is unavailable. When the donor meets any of the three conditions, transplant candidate testing should occur during hospital admission for the organ transplant but prior to implantation of the organ, unless the transplant candidate is known through prior testing to be infected. (Category IB)

17. Pre-transplant testing of transplant candidates for HBV or HCV should be conducted when the donor (living or deceased) is known to be infected with HBV or HCV. Transplant candidate testing should occur during hospital admission for the organ transplant but prior to organ implantation, unless the transplant candidate is known through prior testing to be infected. (Category IB)

18. Posttransplant HBV testing of recipients should be conducted when the donor (living or deceased) meets any of the following conditions: (1) identified as being at increased risk for HBV infection, (2) screening specimens are hemodiluted, (3) the medical/behavioral history is unavailable, or (4) the donor is infected with HBV. Recipient testing should be performed sometime between one and three months posttransplant to include HBV NAT and HBsAg, and at 12 months posttransplant to include antibody to hepatitis B surface antigen (anti-HBs), anti-HBc, and either HBV NAT or HBsAg (unless infection was documented pre-transplant). (Category IB)

19. Posttransplant HIV testing of recipients should be conducted when the donor (living or deceased) meets any of the following conditions: (1) identified as being at increased risk for HIV infection, (2) screening specimens are hemodiluted, or (3) the medical/behavioral history is unavailable. Recipient testing should be performed sometime between one and three months posttransplant to include HIV NAT or an HIV Ag/Ab combination assay (unless infection was documented pre-transplant). NAT or an Ag/Ab combination assay for HIV detection is important as infected recipients may remain Ab-negative due to immunosuppression. (Category IB)

20. Posttransplant HCV testing of recipients should be conducted when the donor (living or deceased) meets any of the following conditions: (1) identified as being at increased risk for HCV infection, (2) screening specimens are hemodiluted, (3) the medical/behavioral history is unavailable, or (4) the donor is infected with HCV. Recipient testing should be performed sometime between one and three months posttransplant to include HCV NAT (unless infection was documented pre-transplant). NAT is important for HCV detection as infected recipients may remain Ab-negative due to immunosuppression. (Category IB)

Refer also to Figure 6 in the original guideline document for re- and posttransplant recipient test recommendations.

Collection and/or Storage of Donor and Recipient Specimens

21. For deceased donors, the Organ Procurement Organization (OPO) should consider collecting two blood specimens, when possible, for HIV, HBV, and HCV real-time testing (i.e., prior to organ recovery)—an ethylenediaminetetraacetic acid (EDTA) plasma specimen or serum specimen for serologic assays and a separate EDTA plasma specimen for NAT. Additionally, the OPO should consider collecting two blood specimens for archiving, when possible. If it is only feasible to collect one specimen, a plasma specimen collected in EDTA, rather than a serum specimen, is optimal. (Category IIB)

22. The OPO should consider archiving blood specimens from deceased donors for at least 10 years. (Category IIB)

23. For living donors, transplant candidates, and recipients, two blood specimens should be collected when HIV, HBV, or HCV testing is planned —an EDTA plasma specimen or serum specimen for serologic assays and a separate EDTA plasma specimen for NAT. (Category IB)

24. Infusion of crystalloid and colloid solutions and transfusion of blood products can cause hemodilution and produce false-negative results for HIV, HBV, and HCV testing. Therefore, the OPO should make an effort to collect a qualified (non-hemodiluted) specimen—that is, a specimen that is deemed acceptable for testing according to an appropriate hemodilution algorithm and calculation method, such as provided by the U.S. Food and Drug Administration (FDA). Furthermore, a hemodilution calculation should be performed on archived specimens of deceased donors to facilitate interpretation of test results. (Category IB)

25. All stored blood vessel conduits from a donor found to be infected with HIV, HBV, or HCV should be quarantined immediately and not released for clinical use unless the HBV- or HCV-infected vessel conduits are needed for the initial transplant procedure in the recipient. After completing the initial transplant procedure, any remaining vessel conduits should be disposed of in accordance with hospital policy to prevent inadvertent release from quarantine and unintentional use in other patients. (Category ID)

Tracking and Reporting of HIV, HBV, and HCV

26a. When an OPO receives information before organ recovery that a deceased potential donor is at increased risk for or is infected with HIV, HBV, or HCV, the OPO should notify (1) the Organ Procurement and Transplantation Network (OPTN), (2) the transplant centers receiving organ offers, and (3) any institutions considering tissue and eye recovery. (Category IB)

26b. The OPO should also notify the public health authorities where the potential donor is admitted, in accordance with state requirements for

reporting notifiable infections, if the deceased potential donor is infected. (Category IC)

27a. When an OPO receives information after organ recovery that a deceased donor was infected with HIV, HBV, or HCV, or that an organ recipient infection with HIV, HBV, or HCV is suspected of being donor-derived, the OPO should notify (1) the OPTN, (2) the transplant centers that received organs and/or blood vessel conduits from the deceased donor, and (3) any institutions that recovered tissues and eyes from the donor. (Category IB)

27b. The OPO should also notify public health authorities where the organ recovery took place, in accordance with state requirements for reporting notifiable infectious diseases, if the deceased donor was infected. (Category IC)

28a. When a transplant center receives information that a recipient of an organ or blood vessel conduit from any deceased donor is newly infected with HIV, HBV, or HCV posttransplant and the infection is suspected of being donor-derived, the transplant center should notify (1) the OPTN and (2) the OPO that procured the organs and any blood vessel conduits. (Category IB)

28b. In accordance with state requirements for reporting notifiable infectious diseases, the transplant center where the transplant took place should also notify public health authorities of the recipient infection. (Category IC)

29a. When a living donor recovery center receives information before organ recovery that a living potential donor is infected with HIV, HBV, or HCV, the living donor recovery center should notify the transplant center intended to receive the organ. If the organ from an HBV- or HCV-infected donor is used for transplantation, the living donor recovery center should also notify the OPTN. (Category IB)

29b. In accordance with state requirements for reporting notifiable infectious diseases, the living donor recovery center should also notify public health authorities where the potential donor lives of the potential living donor's infection. (Category IC)

30a. When a living donor recovery center receives information after organ recovery that a living donor is infected with HIV, HBV, or HCV, the living donor recovery center should notify (1) the OPTN and (2) the transplant center that received an organ from the living donor. Disclosure to the OPTN and transplant center should be in accordance with state requirements. (Category IB)

30b. In accordance with state requirements for reporting notifiable infectious diseases, the living donor recovery center should also notify public health authorities where the organ recovery took place of the living donor's infection. (Category IC)

31. When a living donor recovery center receives information after organ recovery that an organ recipient infection with HIV, HBV, or HCV is suspected of being donor-derived, the living donor recovery center should notify the OPTN. (Category IB)

32a. When a transplant center receives information that a recipient of an organ from a living donor is newly infected with HIV, HBV, or HCV posttransplant and the infection is suspected of being donor-derived, the transplant center should notify (1) the OPTN and (2) the living donor recovery center that procured the organ. (Category IB)

32b. In accordance with state requirements for reporting notifiable infectious diseases, the transplant center should also notify public health authorities where the transplant took place of the recipient's infection. (Category IC)

33. A living donor whose blood specimen is positive for HIV, HBV, or HCV when tested by the living donor recovery center should be notified by the living donor recovery center of his or her infectious disease status. (Category ID)

34. OPOs should have a system in place allowing tracking between a common deceased donor and (1) recovered organs, (2) recovered associated blood vessel conduits, and (3) recovered tissues and eyes to facilitate notification when a donor-derived disease transmission is suspected. This system should include accurate records of the distribution and disposition of each organ and initial distribution of associated blood vessel conduits, along with procedures to facilitate the timely notification of transplant centers and tissue and eye recovery establishments when a donor-derived disease transmission is suspected. To facilitate notification by the OPO, transplant centers should keep accurate records of all organs and associated blood vessel conduits received and the disposition of each. (Category ID).

Definitions:

Categorization Scheme

Category	Recommendation Strength and Quality of Evidence
Category IA	Strong recommendation supported by high- to moderate-quality evidence suggesting net clinical benefits or harms

Recommendation Strength and Quality of Evidence	
Category IB	Strong recommendation supported by low- to very low-quality evidence suggesting net clinical benefits or harms
Category IC	Strong recommendation required by state or federal regulation, regardless of evidence quality
Category ID	Recommendation from a previously published guideline or report not linked to a key question and no systematic review of the literature performed, but the critical outcome considered was determined to result in a net benefit, regardless of evidence quality
Category IIA	Weak recommendation supported by high- to moderate-quality evidence suggesting a trade-off between clinical benefits and harms
Category IIB	Weak recommendation supported by low- to very low-quality evidence suggesting a trade-off between clinical benefits and harms

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) infection transmitted through organ transplantation

Guideline Category

Counseling

Evaluation

Prevention

Risk Assessment

Screening

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Pathology

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Clinical Laboratory Personnel

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To improve organ transplant recipient outcomes by reducing the risk of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission, keeping in mind that transplantation can never be free of this risk
- To provide guidance to organ procurement organization (OPO) personnel; transplant center personnel, including physicians, nurses, administrators, and clinical coordinators; laboratory personnel responsible for testing and storing donor and recipient specimens; and individuals responsible for developing, implementing, and evaluating infection prevention and control programs for OPOs and transplant centers

Target Population

Adult and pediatric donors who are living or deceased, as well as transplant candidates and recipients

Interventions and Practices Considered

1. Risk assessment (screening) of living and deceased donors for human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) infection
2. Testing of living and deceased donors for HIV, HBV, and HCV
    - Testing for antibodies to HIV (i.e., anti-HIV 1/2 or HIV antigen/antibody [Ag/Ab] combination assay)
    - Testing for HIV ribonucleic acid (RNA) by nucleic acid test (NAT) or HIV antigen (e.g., HIV Ag/Ab combination assay)
    - Testing for both anti-HCV and for HCV RNA by NAT
    - Testing for antibody to hepatitis B core antigen (anti-HBc) and for hepatitis B surface antigen (HBsAg)
3. Informed consent discussion with transplant candidate or medical decision maker that includes providing risk information about HIV, HBV, HCV infection
4. Collection and/or storage of donor and recipient specimens
    - Ethylenediaminetetraacetic acid (EDTA) plasma specimens
    - Serum specimens
5. Tracking and reporting of HIV, HBV, and HCV

Major Outcomes Considered

- Prevalence and incidence of human immunodeficiency virus (HIV) and hepatitis B and C among deceased and living organ donors
- Transmission rates
- Sensitivity and specificity of diagnostic tests
- Behavioral and nonbehavioral risk factors associated with an increased probability of infection
- Survival/Mortality
- Graft survival
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Development of Key Questions

The Methodology Working Group first conducted an electronic search of the Agency for Healthcare Research and Quality's National Guideline Clearinghouse®, the National Library of Medicine's MEDLINE® database, EMBASE®, and the Cochrane® Health Technology Assessment Database. They then contacted experts to identify existing national and international guidelines and reviews relevant to human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission in organ transplantation. A preliminary list of key questions was developed from a review of the relevant guidelines and reviews were identified in the search. Key questions were put in final form after vetting them with the Expert Panel and Review Committee. An analytical framework depicting the relationship among the key questions is included in Figure 9 in the original guideline document.

Literature Search

Following the development of the key questions, search terms were developed to identify the literature that was most relevant to those questions. For quality assurance purposes, these terms were compared with those used in relevant seminal studies and reviews. These search terms were then incorporated into search strategies for the relevant electronic databases. Searches were performed in EMBASE, The Cochrane Library Databases, the National Library of Medicine's PREMEDLINE® and MEDLINE, the Agency for Healthcare Research and Quality's National Guideline Clearinghouse, and the ECRI Institute Healthcare Standards Directory. Resulting references were imported into a citation management database where duplicates were resolved; the database was last updated on June 30, 2009. Mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and grey literature (i.e., reports, studies, articles, and monographs that do not appear in the peer-reviewed journal literature and are produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations). The detailed search strategy used to identify primary literature can be found in the Evidence Report (see the "Availability of Companion Documents" field).

Study Selection

Titles and abstracts from references were screened by a single reviewer from ECRI. Full-text articles were retrieved if they were relevant to one or more key questions and met inclusion criteria (i.e., universal as well as question-specific criteria). Universal criteria included studies that were written in English; were peer-reviewed, full-length publications with original data; and included HIV, HBV, or HCV with determination of the infection based on laboratory test(s) rather than subjective estimates, physician interviews, or patient interviews. Additional criteria applied on a per-question basis are depicted in Figure 10 of the original guideline document.

Multiple publications of the same study were treated as a single study rather than as multiple studies to avoid double-counting patients. Two independent reviewers from ECRI screened full-text articles and resolved disagreements through discussion. The results of this process are shown in Figure 11 of the original guideline document. To ensure that all relevant studies were captured in the search, the Expert Panel and Review Committee vetted the bibliography.

The specific tests of interest for Key Question 5 (What are the test characteristics of the screening methods available to detect HIV, HBV, and HCV in potential organ donors? Do test characteristics differ in particular populations and with donor clinical status [i.e., heart-beating vs. non-heart-beating donors or adult vs. pediatric donors]?) are listed in Figure 7 in the original guideline.

Number of Source Documents

A total of 167 articles met the inclusion criteria. Refer to Figure 11 in the original guideline document for details.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall GRADE* of Evidence Base for Outcome

High—further research is very unlikely to change confidence in the estimate of effect.

Moderate—further research is likely to affect confidence in the estimate of effect and may change the estimate.

Low—further research is very likely to affect confidence in the estimate of effect and is likely to change the estimate.

Very low—any estimate of effect is very uncertain.

*Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Scheme

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction and Synthesis

For those studies meeting inclusion criteria, a single reviewer from ECRI extracted the data into evidence tables. The remaining Methodology Working Group members resolved any disagreements regarding inclusion. Data and analyses were extracted as originally presented in the included studies and displayed in evidence tables for each question. For the purposes of the review, the Working Group defined statistical significance as $p \leq 0.05$.

Grading of Evidence

First, the quality of each study included was assessed using the quality assessment criteria (adapted from existing instruments for quality assessment) (see Figure 12 in the original guideline document). Next, the Methodology Working Group assessed the evidence bases described in the evidence tables for each key question using methods adapted from Grading of Recommendations Assessment, Development and Evaluation (GRADE). GRADE tables were developed for each of the key questions and included any outcomes listed in the evidence tables that were judged to be clinically important, the quantity and type of evidence for each outcome, the relevant findings, and the GRADE of evidence for each outcome.

The initial GRADE of evidence for each outcome was deemed high if the evidence base included a randomized controlled trial (RCT) or a systematic review of RCTs, low if the evidence base included only observational studies, or very low if the evidence base consisted only of expert opinion or uncontrolled studies. The initial GRADE could then be modified by as many as nine criteria. Criteria that could decrease the GRADE of an evidence base included shortcomings in quality (see Figure 12 in the original guideline document), consistency, directness, precision, and publication bias. Criteria that could increase the GRADE included a large magnitude of effect, a dose-response gradient, or inclusion of unmeasured confounders that would increase the magnitude of effect (see Figure 13 in the original guideline document). For questions regarding prevalence, incidence, or rates of transmission from donors to recipients, no RCTs were necessary to address the questions. Therefore, the starting evidence GRADE was high, and the Working Group applied the other components of the GRADE system as appropriate. GRADE definitions are shown in the "Rating Scheme for the Strength of the Evidence" field.

After determining the GRADE of the evidence base for each outcome of a given key question, the Working Group calculated an overall GRADE of the evidence base for any sets of outcomes within the GRADE figure for the key question. The overall GRADE was based on the GRADE category occurring most often for the outcomes deemed critical to making a recommendation; if more than one GRADE category occurred at the same count, the overall GRADE was based on the lowest GRADE. For questions that had outcomes that were not deemed critical by the Methodology Working Group, no overall GRADE was assigned to the evidence.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Recommendations related to the 10 key questions were based on a targeted, systematic review of the best available evidence on reducing human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) infection transmitted through organ transplantation. A modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to provide explicit links between the available evidence and the resulting recommendations. The guideline development process is outlined in Figure 8 in the original guideline document.

Development of the guideline involved participation by multiple groups. The Methodology Working Group included staff from the Centers of Disease Control and Prevention (CDC) Office of Blood, Organ, and other Tissue Safety in the Division of Healthcare Quality Promotion; the Center for Evidence-Based Practice at the University of Pennsylvania Health System; and ECRI Institute. This group was accountable for all phases of guideline methodology, including the development of key questions and the Evidence Report, as well as providing the Expert Panel and Review Committee with progress updates. The Expert Panel comprised individuals with subject-matter expertise; assistance was sought from various members of the Expert Panel to address specific issues throughout development of the guideline. The Review Committee was formed to provide stakeholder input from a public health, regulatory, and transplantation perspective for the topics addressed in the guideline, as well as contribution from manufacturers of infectious disease tests. Both the Expert Panel and Review Committee participated in regular updates via conference calls at key steps and provided review and feedback on the key questions, the bibliography resulting from the literature review, the Evidence Report, and the guideline content. The Public Health Service (PHS) Guideline Revision Working Group performed an in-depth review of public comment submitted regarding the draft guideline recommendations and participated in revision of the full document. The PHS Guideline Revision Working Group comprised representatives from the Office of the Assistant Secretary for Health and PHS agencies.

Formulating Recommendations

Narrative evidence summaries were drafted by the guideline authors using the evidence and GRADE tables. One summary was written for each key question. The guideline authors used the narrative evidence summaries to develop guideline recommendations. In some instances, multiple recommendations emerged from a single narrative evidence summary.

Factors determining the strength of a recommendation included the following: (1) the values and preferences used to determine which outcomes were critical, (2) the harms and benefits that emerged by weighing the critical outcomes, and (3) the overall GRADE of the evidence base. A fourth factor, resource use, was not systematically considered. The categorization scheme for recommendations is shown in the "Rating Scheme for the Strength of the Recommendations" field.

If weighing the critical outcomes for a given key question resulted in a net benefit or a net harm, then a Category I recommendation was formulated to recommend strongly for or against the given intervention, respectively. If weighing the critical outcomes for a given key question resulted in a trade-off between benefits and harms, then a Category II recommendation was formulated to recommend that providers or institutions consider the intervention when deemed appropriate.

Category I recommendations are defined as strong recommendations with the following implications:

1. For patients: Most people in the patient's situation would want the recommended course of action and only a small proportion would not; the patient should request discussion if the intervention is not offered.
2. For clinicians: Most patients should receive the recommended course of action.
3. For policy makers: The recommendation may be adopted as policy or is currently part of federal and/or state statutes, regulations, or standards.

Category II recommendations are defined as weak recommendations with the following implications:

1. For patients: Many people in the patient's situation would want the recommended course of action, but many would not.
2. For clinicians: Different choices will be appropriate for different patients, and clinicians must help each patient to arrive at a management decision consistent with her or his values and preferences.
3. For policy makers: Policy-making will require substantial debate and involve many stakeholders.

Levels A and B represent the quality of the evidence underlying the recommendation, with A representing high- to moderate-quality evidence and B representing low- to very low-quality evidence. Level C represents required practices by state or federal regulations, regardless of evidence

quality.

Evidence-based recommendations were compared with those from guidelines identified in the original systematic search and identified four recommendations from the 1994 PHS guidelines for topics not directly addressed by the systematic review of the evidence. These recommendations are included in the Recommendations section, as they were deemed critical to the target users of this guideline. The recommendations were revised to make them applicable to current expected or actual practice. Two recommendations, in response to a 2009 HIV transmission from a living organ donor, were deemed critical to the target users and included in the Recommendations section for the same reason. One recommendation, in response to inadvertent use of an infected blood vessel conduit, was also deemed critical to target users of this guideline. Unlike recommendations informed by the literature search, these recommendations are not linked to a key question and were listed as Level D.

The strength of a Category IA recommendation is equivalent to that of a Category IB, IC, or ID recommendation; it is only the quality of the evidence that makes each category different. Recommendations related to the three expert opinion questions were designated either IB if they represent a strong recommendation or IIB if they represent a weak recommendation because they were based on expert opinion only. Recommendations included from previously published guidelines or reports were designated ID, as the theoretical benefits for each recommendation were clear, regardless of evidence quality.

The wording of each recommendation was carefully selected to reflect the recommendation's strength. When writing Category I recommendations (strong recommendations), phrases such as "should" or "should not" and verbs without conditionals were used to convey certainty. When writing Category II recommendations (weak recommendations), words such as "consider" and phrases such as "may be considered" or "should be considered" were chosen to reflect the lesser certainty of the Category II recommendations. Rather than a simple statement of fact, each recommendation is actionable, describing precisely a proposed action to take. All recommendations focus only on efficacy, effectiveness, and safety. Yet, the optimal use of this guideline should include a consideration of the costs relevant to the local setting of guideline users.

Finalizing the Guideline

After a draft of the tables, narrative summaries, and recommendations was completed, the guideline authors shared the draft guideline with the Expert Panel and Review Committee and made revisions to the guideline based in part on their feedback.

Rating Scheme for the Strength of the Recommendations

Categorization Scheme*

Category	Recommendation Strength and Quality of Evidence
Category IA	Strong recommendation supported by high- to moderate-quality evidence suggesting net clinical benefits or harms
Category IB	Strong recommendation supported by low- to very low-quality evidence suggesting net clinical benefits or harms
Category IC	Strong recommendation required by state or federal regulation, regardless of evidence quality
Category ID	Recommendation from a previously published guideline or report not linked to a key question and no systematic review of the literature performed, but the critical outcome considered was determined to result in a net benefit, regardless of evidence quality
Category IIA	Weak recommendation supported by high- to moderate-quality evidence suggesting a trade-off between clinical benefits and harms
Category IIB	Weak recommendation supported by low- to very low-quality evidence suggesting a trade-off between clinical benefits and harms

*See also the "Description of Methods Used to Formulate the Recommendations" field for methods used to determine recommendation strength.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The draft guideline was posted on the Federal Register for public comment. The Public Health Service (PHS) Guideline Revision Working Group participated in the revision of the guideline recommendations in consideration of public comment and provided feedback on the full document. The draft guideline was then shared with the Expert Panel and Review Committee for technical considerations. Finally, the Office of the Assistant Secretary for Health (OASH) submitted the guideline for review and approval by Department of Health and Human Services (HHS). The opinions of individual members of the Expert Panel or Review Committee might not be fully reflected in this document, as the guideline represents the position of the PHS agencies and is not a consensus document.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Recommendations in these guidelines are based on scientific evidence and expert opinion.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Reduced risk of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission during organ transplantation resulting in improved outcomes for organ transplant recipients
- Benefits of routine testing of recipients who receive organs from increased-risk donors include early identification of infection and treatment before signs and symptoms develop, as well as early notification of recipients of organs from the same donor should a donor-derived infection be suspected.

Potential Harms

- Human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission
- False-positive and false-negative tests

Qualifying Statements

Qualifying Statements

- Given the large discrepancy between the number of candidates on the transplant list and the number of organs available, recommendations in this document may differ from policies or regulations in the setting of blood or tissue donation, due to different risk and benefit considerations for organ transplantation. Even though attempts should be made to ensure the highest level of safety, organ donor and recipient selection practices and policies should not be restrictive, considering the clinical need. Therefore, informed decision-making is an

important part of this process for transplant clinicians and their patients.
- The opinions of individual members of the Expert Panel or Review Committee might not be fully reflected in this document, as the guideline represents the position of the Public Health Service (PHS) agencies and is not a consensus document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Seem DL, Lee I, Umscheid CA, Kuehnert MJ, United States Public Health Service. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep. 2013 Jul;128(4):247-343. PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Developer(s)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

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Guideline Committee

Expert Panel

Review Committee

PHS Guideline Revision Work Group

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rogers MF, Simonds RJ, Lawton KE, Moseley RR, Jones WK. Guidelines for preventing transmission of human immunodeficiency virus through transplantation of human tissue and organs. MMWR Recomm Rep 1994;43(RR-8):1-17.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the Public Health Reports Web site .

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

Availability of Companion Documents

The following is available:

- Solid organ transplantation and the probability of transmitting HIV, HBV, or HCV: a systematic review to support an evidence-based guideline. 2010 Apr 14. 530 p. Electronic copies: Available in Portable Document Format (PDF) from the Centers for Disease Control and Prevention Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 11, 2013.

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